

# SPL ER/DL Team

## Aug 3, 2011

### Minutes

Teleconference information:

USA Toll-Free 866-213-2145

Access code: 273 8216

Chair for this meeting: Pat Cowall

To do:

- Pat to contact DRLS:
  - o Questions/issues with the current NDC directory – see #2 below for question and response from Paul Loebach.
  - o Possibility for a future teleconference about new NDC directory.
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- Pat to send out request for questions/topics to discuss at a future meeting in August to discuss the new NDC directory and old NDC directory.

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#### 1. DUNS number issues

Dragan: Establishment registrations and DUNS numbers. We are currently working through an issue or maybe many issues related to Dun and Bradstreet updating their information which caused our file to fail validation. When we search DNB we found it seems to depend how you search and which DNB database or tool you use to search, you get different answers. If anyone has a good way to manage this information in DNB perhaps they can share.

Jean: I have had a horrible time with D&B over the last few months. Their response time is totally unacceptable and they just removed one of my site DUNS from the system because they thought it was a duplicate...but they never asked us! So, I failed SPL validation and all our records (applications) that reflected the old number will now require revision.

Jean (Hospira): March – got failure on 4 sites. Contacted D&B to verify the sites. One site was not in the D&B database. Contacted rep for D&B...got corrected information. July – teleconference.

- Australian site was deleted because they thought it was a duplicate with another site. Incorrect. Not a duplicate. They added a new DUNS...and now they need to update all the relevant files.
- Different D&B offices have different rules. Wanted to add some building numbers because they only owned some buildings in an office park. They wanted only 1 number for the campus.
- Timeliness was horrible.

Dragan (Abbott): Same information submitted since June 2009. Never had a failure. Found threw searching different databases....and get different answers. Different DUNS numbers and slightly different address.

- Problems getting changes that stick.
- What are they trying to match exactly within FDA.
  - o Name must match exactly, but there are some slight exceptions
  - o DUNS name is Abbott Biotechnologies Laboratories
    - Abbott Laboratories
    - Abbott Biotechnologies

- Abbreviations are ok.
  - Zip must match exactly
- They are constantly updating their database...tweaking just enough to cause a validation
- This creates issues with
- Suggestion: Because FDA chose D&B, then could D&B add a flag that indicates that this is being used for regulatory purposes, or that the data shouldn't be changed without contacting the corporate officers.

Pat (Lilly): Several of our addresses have changed since we corrected them initially in 2009. Worked with our Corporate Rep to get connected to the D&B data group who eventually corrected them.

- Also asked for / received our D&B "Family tree" printout of all addresses
- Learned that there are different databases. The family tree printout is NOT the database used in the SPL validation process.
- Request: would like D&B contact someone at corporate before they change information?

Ruth: Concur with everyone. D&B has said that they now have kicked up their review

- They continually make changes.
- What are the implications of the new initiative on Foreign Drug Firm Registration Verification by Dun & Bradstreet.
  - Will our addresses be changing again.

Ann: Takeda also has an example to share where D&B told us that they could not correct the spelling of one of our addresses due to a translation from Japanese. Don't know why proper names are being translated but we have had a heck of time getting our ECR through and now it requires an update to add a facility.

**To do: Invite the eDRLS office to our teleconference with the D&B**

## 2. New NDC directory:

- a. Elimination of inner packaging from the NDC directory
  - i. Corporate reimbursement groups are very concerned because the inner pack (especially hospital packs) is needed for reimbursement.
  - ii. Medicare coverage gap discount agreement – states all NDCs must be electronically listed. Thus CMS is saying that if an NDC code is not in the new NDC directory, it won't be reimbursed. ie CMS won't use the old NDC directory to reimburse. Do we have a problem here with reimbursements?
  - iii. Did DRLS interact with CMS before eliminating the publishing of inner packs.
  - iv. **Response from Paul Loebach:**
    - Yes, The groups actually did interact, but they didn't understand the implications of
      - a. CMS requiring NDC to be included in NDC directory and
      - b. DRLS eliminating the inner packs from the NDC directory.
    - DRLS understands the issue and they are meeting on Friday Aug 5<sup>th</sup> to discuss the issue, in light of the problems that this is causing.
    - Workaround is to drug list the individual reimbursable units separately – ie at the pack level.
- b. Some of the things that we electronically drug listing using the terms back then did not migrate over to the new database.
  - i. Ask DRLS group why they weren't in the new NDC directory.

- ii. They didn't they appear because they were drug listed using an outdated doc type of Human Prescription...with Highlights. Need to drug list it again for it to appear in the new NDC directory.
  - iii. Response from Paul Loebach:
    - Some sponsors drug listed in R4 using the old doc type. Many of these files are missing some key data. Thus, FDA determined that these files should be updated with the current doc type and resubmitted -- where they can be validated using current validation standards.
    - Note: For these same reasons, FDA also is encouraging sponsors to update their R3 SPL to R4 -- ie to drug listing electronically.
3. Ruth: FYI. They received notification from DRLS that they were reviewing certain products and wanted them to drug list both the manufacturer (ie manufactured for PLD) and PLD. Domestic situation.
- a. They drug listed both before June 1...and both sets on NDC codes were in the NDC directory and Daily Med.
  - b. Contacted DLRS and they pulled both out of NDC directory.
  - c. They are in the process of fixing it. Ruth will report back.

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Outstanding questions from previous teleconferences – for future discussion.

- 4. Please discuss the suggestion of including lot distribution data in the SPL file. How can this be accomplished? Will an SPL file have to be updated at each lot release? – Jean
- 5. We currently use the campus approach for our manufacturing facility at our corporate center. We are currently trying to assess the possibility (and value) of subdividing the campus into smaller sub-sites, based on manufacturing functional -- ie API, dry products, and parenteral. - Pat
- 6. Are companies adding alternate testing sites for drug substances to the Labeler and Manufacturer Information section of the SPL or just adding the API supplier to the Labeler and Manufacturer Information section of the SPL? – Kathleen
- 7. Has anyone received the following packaging validation error even though there are no drug listing differences in the SPL since the last posted SPL: "If the NDC Package Code has been previously submitted, then the package form code and quantity value and unit must be the same as in the most recent submission for this NDC code". – Amy
- 8. In a situation where a CBE is changed to a PAS, and the CBE version of the circular is pulled back and replaced with the previous version while the PAS is pending, what is the process for replacing the eListed SPL with the previous version? Can we revert back to the previous SPL version we already submitted? Or do we need to resubmit that SPL as a new version with new version number and rootID? Also, is there a defined period of time after a CBE is submitted that FDA has to tell a sponsor to change a CBE to a PAS? - Amy
- 9. There are two examples of Drug Listing Data for products that use the term "equivalent to" and want to see how other companies are portraying this information. - Kathleen

Have seen similar “equivalent to” information in labels and see other companies portray this information different than our company does:

- a. Example 1: Description section states, “Each mL contains 118 mcg of dexmedetomidine hydrochloride equivalent to 100 mcg of dexmedetomidine”. Drug Listing Data looks like this:

Active Ingredient/Active Moiety:

Ingredient Name: **DEXMEDETOMIDINE HYDROCHLORIDE** (Dexmedetomidine)

Basis of Strength: Dexmedetomidine

Strength: 100 ug in 1 mL

In this case does it matter whether you use 118 mcg/mL and choose dexmedetomidine hydrochloride as the basis of strength?

- b. Example 2: Description section states, “The vials contain sterile vancomycin hydrochloride equivalent to either 500 mg or 1 g vancomycin activity.”. Drug Listing Data looks like this

Active Ingredient/Active Moiety:

Ingredient Name: **VANCOMYCIN HYDROCHLORIDE** (VANCOMYCIN)

Basis of Strength: VANCOMYCIN

Strength: 500 mg in 10 mL or 1 g in 20 mL

In this case does it matter whether you use 118 mcg/mL and choose dexmedetomidine hydrochloride as the basis of strength?

10. My boss is expressing concern over these new document types (I thought I was going to have to give her CPR). Lonnie has requested that we switch our Kogenate antihemophilic factor (recombinant) to the plasma derived template. The templates listed below will be available in the newest i4i release set for June 5th. Please see her comments below.

#### New SPL Document Types

- CELLULAR THERAPY
- CELLULAR THERAPY with highlights
- PLASMA DERIVATIVE
- PLASMA DERIVATIVE with highlights
- LICENSED VACCINE BULK INTERMEDIATE LABEL
- LICENSE BLOOD INTERMEDIATES/PASTE LABEL
- STANDARDIZED ALLERGENIC
- STANDARDIZED ALLERGENIC with highlights

"To have any classification or categorization of recombinant products as plasma-derived products without a recombinant distinction can be quite problematic. As the SPL is posted publicly, can be downloaded by anyone with access to the internet, yet can easily misinterpret the evolving and complex data associated with these files, it is of great concern that someone could misunderstand that this recombinant product is somehow also viewed as a plasma-derived product. This immediately brings to mind the valid concerns and problems of plasma-derived products during the 1990s where some used plasma containing infectious disease elements before certain infectious diseases were better understood. There are countries that depend upon the FDA-associated documentation of US approved biologics, yet are only beginning to introduce recombinant products into their countries.

The below statement is from the FDA - CBER website on a project page "Towards More Effective Treatment for Blood Clotting Disorders: Pharmacogenetics of von Willebrand Factor (vWF) and Related Proteins":

<http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm127059.htm>

The Division of Hematology is responsible for the evaluation of biologic products related to blood. Among these products are recombinant coagulation factors that are substitutes for their plasma-derived counterparts.

If it is a matter of naming a document type or template, please consider adding "recombinant" or changing to "factors". Please do not limit the name to 'plasma derived'."

**Followup with outcomes:**

- Paula Finn: problems with establishment information for "campuses" and French.